

Amendments to the Specification

Please delete paragraph [0157] of the specification and replace it with the following paragraph.

Sites that may be used in the present invention include att sites. The 15 bp core region of the wild-type att site (GCTTTTTTAT ACTAA (SEQ ID NO:1)), which is identical in all wild-type att sites, may be mutated in one or more positions. Other att sites that specifically recombine with other att sites can be constructed by altering nucleotides in and near the 7 base pair overlap region, bases 6-12 of the core region. Thus, recombination sites suitable for use in the methods, molecules, compositions, and vectors of the invention include, but are not limited to, those with insertions, deletions or substitutions of one, two, three, four, or more nucleotide bases within the 15 base pair core region (see U.S. Application Nos. 08/663,002, filed June 7, 1996 (now U.S. Patent No. 5,888,732) and 09/177,387, filed October 23, 1998, which describes the core region in further detail, and the disclosures of which are incorporated herein by reference in their entireties). Recombination sites suitable for use in the methods, compositions, and vectors of the invention also include those with insertions, deletions or substitutions of one, two, three, four, or more nucleotide bases within the 15 base pair core region that are at least 50% identical, at least 55% identical, at least 60% identical, at least 65% identical, at least 70% identical, at least 75% identical, at least 80% identical, at least 85% identical, at least 90% identical, or at least 95% identical to this 15 base pair core region.

Please delete paragraph [0160] of the specification and replace it with the following paragraph. Note that the underlined nucleotides in the sequence were present in the application as filed. The underlining is a method of identifying a particular portion of the sequence and does not represent the addition of new matter.

The core sequence of each att site (attB, attP, attL and attR) can be divided into functional units consisting of integrase binding sites, integrase cleavage sites and sequences that determine specificity. Specificity determinants are defined by the first three positions following the integrase top strand cleavage site. These three positions are shown with underlining in the following reference sequence: CAACTTTTTTATAC AAAGTTG (SEQ

ID NO:2). Modification of these three positions (64 possible combinations, Table 16) can be used to generate att sites that recombine with high specificity with other att sites having the same sequence for the first three nucleotides of the seven base pair overlap region. The possible combinations of first three nucleotides of the overlap region are shown in Table 16.

Please delete paragraph [0163] of the specification and replace it with the following paragraph.

For example, mutated att sites that may be used in the practice of the present invention include attB1 (AGCCTGCTTT TTTGTACAAA CTTGT (SEQ ID NO:3)), attP1 (TACAGGTACAC TAATACCATC TAAGTAGTTG ATTCATAGTG ACTGGATATG TTGTGTTTA CAGTATTATG TAGTCTGTTT TTTATGCAAA ATCTAATTAA ATATATTGAT ATTTATATCA TTTTACGTTT CTCGTTCAAGC TTTTTGTAC AAAGTTGGCA TTATAAAAAAA GCATTGCTCA TCAATTGTT GCAACGAACA GGTCACTATC AGTCAAAATA AAATCATTAT TTG (SEQ ID NO:4)), attL1 (CAAATAATGA TTTTATTTG ACTGATAGTG ACCTGTTCGT TGCAACAAAT TGATAAGCAA TGCTTTTTA TAATGCCAAC TTTGTACAAA AAAGCAGGCT (SEQ ID NO:5)), and attR1 (ACAAGTTGT ACAAAAAAGC TGAACGAGAA ACGTAAAATG ATATAAATAT CAATATATTA AATTAGATT TGCAAAAAA ACAGACTACA TAATACTGTA AAACACAAACA TATCCAGTCA CTATG (SEQ ID NO:6)). Table 18 provides the sequences of the regions surrounding the core region for the wild type att sites (attB0, P0, R0, and L0) as well as a variety of other suitable recombination sites. Those skilled in the art will appreciate appreciated that the remainder of the site may be the same as the corresponding site (B, P, L, or R) listed above.

Please delete paragraph [0188] of the specification and replace it with the following paragraph.

In some embodiments, it may be desirable to remove all or a portion of a tag sequence from a fusion protein comprising a tag sequence and a polypeptide sequence encoded by a cloned ORF of the invention. In embodiments of this type, one or more amino acids forming a cleavage site, *e.g.*, for a protease enzyme, may be incorporated into the primary sequence of the fusion protein. The cleavage site may be located such that cleavage

at the site may remove all or a portion of the tag sequence from the fusion protein. In some embodiments, the cleavage site may be located between the tag sequence and the sequence of the polypeptide such that all of the tag sequence is removed by cleavage with a protease enzyme that recognizes the cleavage site. Examples of suitable cleavage sites include, but are not limited to, the Factor Xa cleavage site having the sequence Ile-Glu-Gly-Arg (SEQ ID NO:7), which is recognized and cleaved by blood coagulation factor Xa, and the thrombin cleavage site having the sequence Leu-Val-Pro-Arg (SEQ ID NO:8), which is recognized and cleaved by thrombin. Other suitable cleavage sites are known to those skilled in the art and may be used in conjunction with the present invention.

Please delete Table 18 of the specification and replace it with the following Table.

Table 18. Nucleotide sequences of att sites.		
attB0	AGCCTGCTTT TTTATACTAA CTTGAGC	(SEQ ID NO: <u>9</u>)
attP0	GTTCAGCTTT TTTATACTAA GTTGGCA	(SEQ ID NO: <u>10</u>)
attL0	AGCCTGCTTT TTTATACTAA GTTGGCA	(SEQ ID NO: <u>11</u>)
attR0	GTTCAGCTTT TTTATACTAA CTTGAGC	(SEQ ID NO: <u>12</u>)
attB1	AGCCTGCTTT TTTGTACAAA CTTGT	(SEQ ID NO: <u>3</u>)
attP1	GTTCAGCTTT TTTGTACAAA GTTGGCA	(SEQ ID NO: <u>13</u>)
attL1	AGCCTGCTTT TTTGTACAAA GTTGGCA	(SEQ ID NO: <u>14</u>)
attR1	GTTCAGCTTT TTTGTACAAA CTTGT	(SEQ ID NO: <u>15</u>)
attB2	ACCCAGCTTT CTTGTACAAA GTGGT	(SEQ ID NO: <u>16</u>)
attP2	GTTCAGCTTT CTTGTACAAA GTTGGCA	(SEQ ID NO: <u>17</u>)
attL2	ACCCAGCTTT CTTGTACAAA GTTGGCA	(SEQ ID NO: <u>18</u>)
attR2	GTTCAGCTTT CTTGTACAAA GTGGT	(SEQ ID NO: <u>19</u>)
attB5	CAACTTATT ATACAAAGTT GT	(SEQ ID NO: <u>20</u>)
attP5	GTTCAACTTT ATTATACAAA GTTGGCA	(SEQ ID NO: <u>21</u>)
attL5	CAACTTATT ATACAAAGTT GGCA	(SEQ ID NO: <u>22</u>)

Table 18. Nucleotide sequences of att sites.

attR5	GTTCAACTT ATTATACAAA GTTGT	(SEQ ID NO: <u>23</u>)
attB11	CAACTTTCT ATACAAAGTT GT	(SEQ ID NO: <u>24</u>)
attP11	GTTCAACTT TCTATACAAA GTTGGCA	(SEQ ID NO: <u>25</u>)
attL11	CAACTTTCT ATACAAAGTT GGCA	(SEQ ID NO: <u>26</u>)
attR11	GTTCAACTT TCTATACAAA GTTGT	(SEQ ID NO: <u>27</u>)
attB17	CAACTTTGT ATACAAAGTT GT	(SEQ ID NO: <u>28</u>)
attP17	GTTCAACTT TGTATACAAA GTTGGCA	(SEQ ID NO: <u>29</u>)
attL17	CAACTTTGT ATACAAAGTT GGCA	(SEQ ID NO: <u>30</u>)
attR17	GTTCAACTT TGTATACAAA GTTGT	(SEQ ID NO: <u>31</u>)
attB19	CAACTTTTC GTACAAAGTT GT	(SEQ ID NO: <u>32</u>)
attP19	GTTCAACTT TTCTACAAA GTTGGCA	(SEQ ID NO: <u>33</u>)
attL19	CAACTTTTC GTACAAAGTT GGCA	(SEQ ID NO: <u>34</u>)
attR19	GTTCAACTT TTCTACAAA GTTGT	(SEQ ID NO: <u>35</u>)
attB20	CAACTTTTG GTACAAAGTT GT	(SEQ ID NO: <u>36</u>)
attP20	GTTCAACTT TTGGTACAAA GTTGGCA	(SEQ ID NO: <u>37</u>)
attL20	CAACTTTTG GTACAAAGTT GGCA	(SEQ ID NO: <u>38</u>)
attR20	GTTCAACTT TTGGTACAAA GTTGT	(SEQ ID NO: <u>39</u>)
attB21	CAACTTTTA ATACAAAGTT GT	(SEQ ID NO: <u>40</u>)
attP21	GTTCAACTT TTAATACAAA GTTGGCA	(SEQ ID NO: <u>41</u>)
attL21	CAACTTTTA ATACAAAGTT GGCA	(SEQ ID NO: <u>42</u>)
attR21	GTTCAACTT TTAATACAAA GTTGT	(SEQ ID NO: <u>43</u>)

At the end of the specification, just before the claims please insert the text from the file "IVGN334.ST25.txt" submitted herein. This file contains a Sequence listing according 37 C.F.R. §§ 1.821-1.825 and does not constitute the addition of new matter.

